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Case Report

Scrub Typhus-Varied Presentation

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Abstract: Scrub typhus is an acute febrile illness caused by mite-borne Gram-negative bacterium *Orientia tsutsugamushi*. We report a case of Multi organ dysfunction syndrome admitted in Intensive care unit and was diagnosed with Scrub Typhus. Patient was brought in a state of altered sensorium with profuse pink secretion from throat and gasping for breath. As GCS was 4 patient was intubated and kept under mechanical ventilation. History of Diabetes, Hypertension and Ischemic Heart disease from 5 years was noted. Patient had history of fever with chills, cough with expectoration and breathlessness for which she was admitted in local clinic which did not relieve her symptoms. Examination revealed hypotension, cyanosis, clubbing, pedal edema and tachycardia. Systemic examination revealed absent breath sounds in left hemithorax and right basal areas. Chest Radiography suggestive of alveolointerstitial infiltrates of left hemithorax and right lower zone. Arterial blood gas analysis showed acute type1 respiratory failure. Total count was 48,500/ mm^3 and patient had abnormal renal function.Pao2/Fio2 was 180. Weil Felix test was positive with 1:320 dilutions on day 3 and Immunoflorescence assay was positive for IgM antibody. Patient responded to Doxycycline and improved over a period of 8 days. Scrub typhus should be considered as a possibility among patients admitted with Acute Respiratory distress syndrome (ARDS) which is often undiagnosed. Persistence of viable organisms should be evaluated as *O. tsutsugamushi* can cause chronic latent symptomatic infection in spite of antibiotic therapy.
Keywords: Scrub Typhus, Multi organ Dysfunction syndrome, Septic shock, Acute Respiratory distress Syndrome.

INTRODUCTION

Scrub typhus is an acute febrile illness caused by mite-borne Gram-negative bacterium *Orientia tsutsugamushi* of family *Rickettsiaceae*. Scrub typhus or Bush typhus was first isolated and identified in 1930 in Japan [1]. Infection spreads through infected chigger, the larval stage of *Leptotrombidium* mites. They are 6-legged; 0.2-mm larvae are not host specific and feed for 2-10 days on the skin fluids of the host. Wild rats serve as the natural reservoir for the chiggers [2]. It is endemic to the Asia-Pacific region [2, 3, 4]. The tsutsugamushi triangle extends from northern Japan and far-eastern Russia in the north, to the territories around the Solomon Sea into northern Australia in the south, and to Pakistan and Afghanistan in the west [5].

Most cases of Scrub Typhus are undiagnosed, an incidence of 18-23% is revealed through prospective studies in endemic areas [6]. Community surveys in Malaysia reported an incidence of 3.2-3.5% per month and a seroprevalence exceeding 80% in those older than 44 years [7]. Seasonal occurrence of scrub typhus varies with the climate in different countries as mites prefer the rainy season and certain areas like forest clearings, riverbanks, and grassy regions. As there is increased mite activity as the weather warms, cases are recorded earlier in the year from a few years [8].

No differences based on gender or race is documented. The clinical spectrum of the disease is variable, from asymptomatic to fulminant forms, but usually diagnosed with history of mite exposure and eschar on clinical examination. History of travel to endemic area, exposures in rural areas and contact with vegetation or the ground should be recorded [9]. Inoculation by the chigger bite is often painless and unnoticed. The incubation period is from 6-20 days.

Early lymphopenia with late lymphocytosis, decrease in the CD4:CD8 lymphocyte ratio and Thrombocytopenia can be seen. Serologic tests for antibodies are the diagnostic tests of choice. Elevated transaminase levels may be present in 75-95% of patients, Hypoalbuminemia in about 50% of cases but, hyperbilirubinemia is rare. Indirect immunoperoxidase test and immunofluorescent assay are the confirmatory

tests. An infection is confirmed by a 4-fold increase in antibody titers between acute and convalescent serum specimens.

A single high titer with classic clinical features is considered a probable case. Five serotypes i.e. Karp, Gilliam, Kawazaki, Boryon, and Kato are helpful in serologic diagnosis [10]. About half are seropositive to Karp antisera, and approximately one-quarter to antisera against the prototype Gilliam strain. Polymerase chain reaction (PCR) technique in clinical specimens can be used for diagnosis especially in early stages.

CASE REPORT

A 60 year-old woman was bought to Emergency room with severe breathlessness, profuse pink secretion and frothing from mouth with gasping for breath. As GCS was 4/15 patient was intubated and mechanically ventilated in Intensive care unit. History from relatives revealed fever with chills, cough with expectoration and shortness of breath from 5 days for which she was admitted in local clinic and was treated with Ceftriaxone. Past history is significant for Diabetes Mellitus, Hypertension and Ischemic Heart disease from past 5 years with non-compliance for treatment.

As the condition of the patient deteriorated, she was referred to our hospital. Relatives denied illegal drug use or exposure to known infected people with similar illness. Her physical examination during admission was remarkable for fever (40°C), hypotension (BP: systolic 70 mm of hg), cyanosis, clubbing, pedal edema and other signs of Systemic Inflammatory Response Syndrome (SIRS), including increased respiratory (36/min) and heart (140/min) rates. Patient had profuse pink fluid with frothing seen in endotracheal tube along with frank blood for a period of 4 days.

Systemic examination showed dullness on percussion on left hemithorax and right infra scapular, interscapular, axillary and infra axillary areas. Bilateral coarse Crepitations were present. Chest Radiography showed extensive alveolointerstitial infiltrate in Left hemithorax and right lower zone which was compatible with Acute Respiratory distress syndrome (ARDS). Patient was started on antibiotics Piperacillin-Tazobactam 4.5g 8th hourly and Levofloxacin 750mg 24hourly. Patient was also started on Oseltamavir 75mg 12th hourly in view of high prevalence of Swine flu infection in Bangalore. 3 samples of Blood culture and endotracheal tube aspirate for influenza was sent immediately.

Investigations revealed total white blood cell count of 42,100 /mm^3 (Neutrophils 24%, Lymphocytes 70%, Eosinophils 3%, monocytes 3%) ESR 52mm/hr), Hemoglobin of 10mg/dl and platelet count was 99,000. The arterial blood gases had pH of 7.31, a PO2 of 60 mmHg, PCO2 of 35.5mmHg and 17.9 mmol/l of bicarbonate. Renal function test was abnormal with Creatinine of 4.6mg/dl and Blood urea of 100mg/dl. Liver function test was normal. ECG showed tachycardia and ST –T changes in leads 3 and aVF. Echocardiography was normal with ejection fraction of 60%.

Mechanical ventilation was continued with PEEP of 15cm of H20 (maintained between 10-20cm of H2O.Closed suctioning of secretions was done from Endotracheal tube. Condition of patient deteriorated on 2nd day with oliguria, shock and Multiple Organ Dysfunction Syndrome. Patient required blood transfusion, ionotropic support and crystalloids. Patient was given 2 packed RBC transfusion, Dopamine and noradrenaline infusion.

No rash or eschar was noted on examination. At first relatives denied mite exposure but it was later found that she travelled to Kolar 10 days ago, an endemic area for scrub typhus. She had exposure to vegetation near the house where she collected firewood. On day 3 weil- Felix test was reported to be positive with 1:320 dilutions. Immunoflorescence assay was positive for IgM antibody (1:60). Patient was started on intravenous Doxycycline 100mg 12th hourly along with continuation of other antibiotics. Condition of patient improved progressively and radiography revealed reduction in pulmonary infiltrates. Patient was extubated on day 5 with continuation of antibiotics and Doxycycline for a period of 10 days. On day 5 weil-felix test was repeated with a result showing 1: 160 dilutions. All blood cultures as well as serological tests including HIV were negative. On day 8 Total counts was 9000/mm^3, Platelet count was199, 000 and hemoglobin was 10.4g/dl. Patient was discharged with a follow up after 1 week.

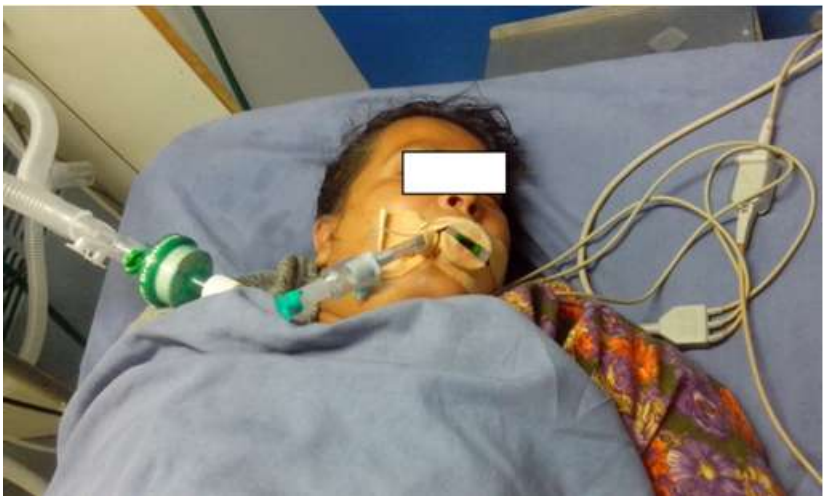

Fig-1: Patient under mechanical ventilation Day 1

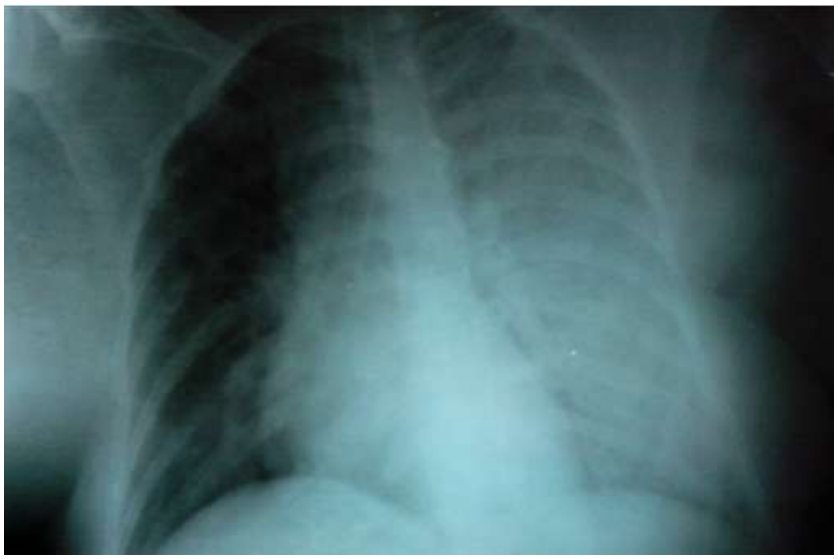

Fig-2: Chest radiography Day 1 showing alveolointerstitial infiltrates

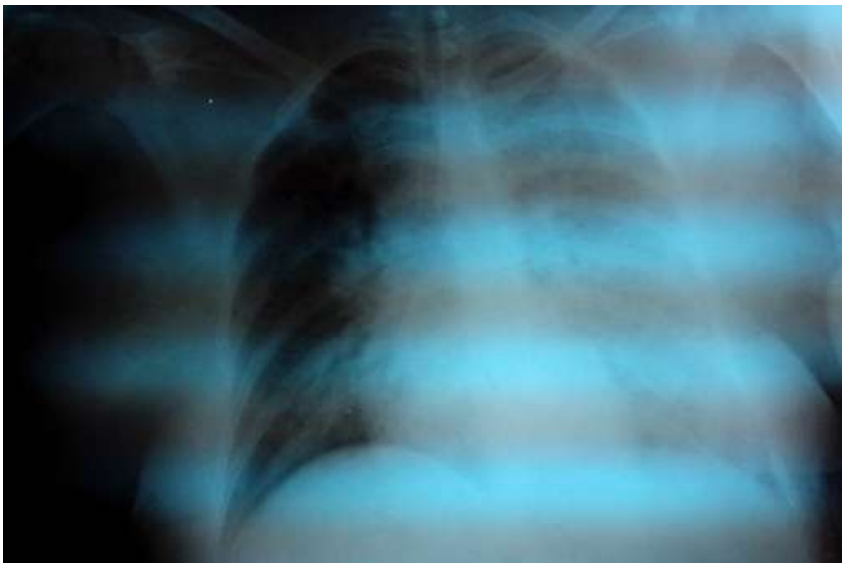

Fig-3: Chest Radiography on Day 2 with alveolointerstitial infiltrates

Fig-4: Patient on day 6 under T-piece ventilation with improved condition

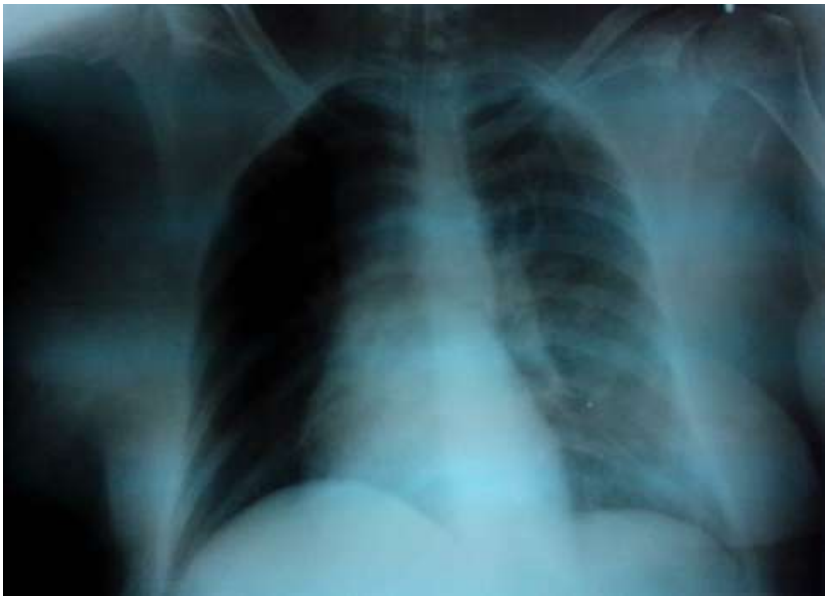

Fig-5: Chest Radiography on Day 4 after starting Doxycycline

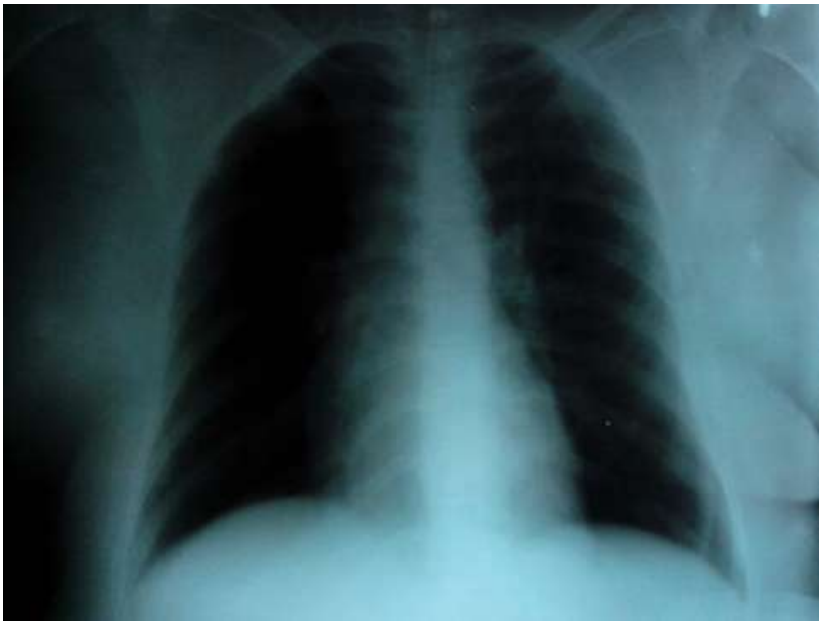

Fig-6: Chest Radiography on Day 6

DISCUSSION

Even though Scrub typhus is prevalent in many parts of India and Asia, specific data is not available.[15] It is grossly under-diagnosed because of its nonspecific presentation, low index of suspicion and the unavailability and affordability of confirmatory diagnostic resources. Scrub typhus is difficult to distinguish clinically from co-endemic diseases such as typhoid, leptospirosis, and dengue. The presence of an eschar is variable. Diagnosis depends on clinical suspicion, prompting the clinician to request an appropriate investigation. Even though weil-felix test is cheap and easily available it is unreliable. Serological methods are most reliable when a fourfold-rise in antibody titre is seen but are expensive. If the patient is from a non-endemic area, diagnosis can be made from a single acute serum sample. Histologically, there is focal or disseminated vasculitis caused by the destruction of endothelial cells and the perivascular infiltration of leukocytes in the lungs showing Pneumonitis in chest radiography.

Current treatment for scrub typhus is administration of a tetracycline (most commonly Doxycycline). Chloramphenicol and macrolides can be used. 7-day antibiotic regimen is effective. Results were mixed on Studies of fluoroquinolones and are not indicated at present.

Failure in diagnosis and delayed therapy has contributed to mortality which is about 15% in some areas. Case fatalities have decreased from 4%–40% to less than 2% with antibiotic treatment. Our patient's presentation is unusual and examination revealed no eschar. Patient improved dramatically with Doxycycline which is evident clinically and radiologically. Infact, rapid resolution of fever following Doxycycline is so characteristic that it can be used as a therapeutic test if there is unavailability of tests or financial constraints. Persistence of viable organisms should be evaluated as *O. tsutsugamushi* can cause chronic latent symptomatic infection in spite of antibiotic therapy.

CONCLUSION

All patients with Fever of unknown origin and acute respiratory distress syndrome should be evaluated for rickettsial infections especially for scrub typhus which is endemic in Asia and is a reemerging infectious disease. If the patient did not respond to prophylactic antibiotic therapy, diagnosis should be re-evaluated to investigate the possibility of scrub typhus as empirical treatment with tetracycline(Doxycycline) is life saving. Investigations should be made available at affordable costs in developing countries where the disease is prevalent.

Preventive measures in endemic areas including protective clothing and insect repellents should be used and awareness among community should be increased regarding the disease. Outbreaks in endemic areas and decreased effectiveness of antibiotic treatment suggest a continued need for a suitable vaccine in near future.

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